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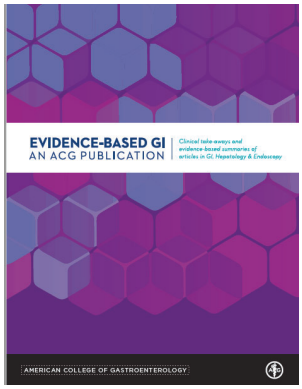

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HEPATOLOGY

Surgery in Cirrhosis: Strategies for Risk Stratification and Optimization

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This summary reviews Mahmud N, Fricker ZP, LM McElroy, et al. ACG Clinical Guideline: Perioperative risk assessment and management in patients with cirrhosis. Am J Gastroenterol 2025;120:1968-1984.

Correspondence: Nikki Duong, MD. Associate Editor. Email: EBGI@gi.org
Keywords: Guideline, cirrhosis, surgery, clinical management

STRUCTURED ABSTRACT

Question: What is the optimal approach to manage perioperative risk in cirrhotic patients undergoing non-hepatic surgical procedures?

Design: A clinical practice guideline developed under the auspices of the ACG Practice Parameters Committee.1 An expert panel of hepatologists, gastroenterologists, and surgeons conducted a systematic literature review and applied the GRADE framework to assess evidence quality and formulate recommendations, following a PICO-based approach.

Setting: Multidisciplinary guideline development sponsored by the ACG, intended for use across all clinical settings (community hospitals, tertiary, and transplant centers) where adults with chronic liver disease undergo surgery.

Patients: Adults with compensated and decompensated cirrhosis undergoing non-hepatic operations (abdominal, cardiothoracic, orthopedic, and others). Patients with

clinically significant portal hypertension (CSPH) were the primary focus. Pediatric patients and liver transplant recipients were excluded

Interventions: Key recommendations include risk:

- Use of cirrhosis-specific calculators (preferably VOCAL-Penn) plus clinical judgement and non-invasive rule-in of CSPH
- Preoperative transplant evaluation should be considered if the projected 90-day mortality is ≥ 15%
- Consideration of transjugular intrahepatic portosystemic shunt (TIPS) when CSPH risk is high and there is another indication for TIPS. Optimize with strict alcohol and tobacco cessation while meeting target nutritional goals (30–35 kcal/kg/day; 1.25–1.5 g/kg/day protein for ≥ 2 weeks).
- Refer to a high-volume liver or transplant-capable center for major procedures when feasible.

Outcomes: The outcomes emphasized in this guideline were: perioperative mortality (particularly 90-day), postoperative hepatic decompensation (new/worsening ascites, hepatic encephalopathy, variceal bleeding), and major complications (infection, wound complications, ICU admission).

Data Analysis: The guideline panel systematically analyzed the available evidence for each clinical question. Using the GRADE methodology, the quality of evidence was rated as high, moderate, low, or very low. Many recommendations in this perioperative domain are based on lower-quality evidence (retrospective studies, cohort data, and expert opinion), since randomized trials in patients with cirrhosis undergoing surgical operations are rare. Strong consensus recommendations were made when the balance of benefit and harm was clear.

Funding: Developed with ACG support. No external or industry funding was utilized.

Results: The guideline provides several recommendations summarized in **Table 1**. In this section, we highlight the most important findings. Initially, the guideline that, to achieve accurate surgical risk stratification, it is recommended to consider three categories of factors: liver-related factors, nonhepatic comorbidities, and surgery-specific factors.

Risk stratification: General scores of liver disease severity are considered insufficient

because they do not capture the complexity of individual procedures; these scores include the CTP and MELD. Among models, the VOCAL-Penn Score is the most reliable predictor of postoperative mortality, with the added benefit of estimating postoperative decompensation within 90 days and being applicable to both hepatic and nonhepatic surgeries.[2] MELD and CTP alone are inadequate, although patients with low MELD scores (6–9) and CTP scores (5–6) seem to have minimal additional risk for low-risk surgeries.[3]

Portal hypertension: CSPH is one of the strongest predictors of postoperative mortality. CSPH is defined as hepatic venous pressure gradient ≥10 mm Hg, liver stiffness measurement (LSM) ≥25 kPa Regardless of platelet count, LSM 20–24.9 kPa with platelet count less than 150K/mm³, or LSM 15–19.9 kPa. with platelet count <110 K/mm³, as well as clear evidence of gastroesophageal varices, portosystemic collaterals, or hepatofugal flow (**Figure 1**).[4]

Etiology: The surgical risk is not directly affected by the cause of cirrhosis, except for MASLD, since it is strongly associated with cardiometabolic comorbidities.[5] The VOCAL-Penn Score incorporates MASLD as a variable,[6] likely serving as a surrogate for cardiometabolic risk. Future studies could investigate the potential interplay between hepatocellular carcinoma,[7] alcohol,[8] viral, or autoimmune liver diseases[9] with surgical risk.

Nutritional status: Malnutrition, sarcopenia, and frailty significantly worsen postoperative outcomes.[10] These factors have been shown to significantly impact post–liver transplant outcomes, though post-transplant mortality itself varies based on transplant type, disease etiology, and other factors.

Other models: In the context of extrahepatic surgery, the Hospital Frailty Risk Score enhances the prediction of postoperative mortality compared to MELD alone,[11] although it does not outperform VOCAL-Penn.The accuracy of the Mayo Surgical Risk Score has decreased over time as it tends to overestimate risk.[2,12]

Procedure-specific guidance and transplant consideration: There are no standardized criteria for initiating liver transplant evaluation before surgery in cirrhosis, but expert guidance suggests consideration when the projected 90-day mortality exceeds 15%.[13] For high-risk patients who may decompensate postoperatively yet do not otherwise meet transplant criteria, completing a transplant evaluation preoperatively can avoid unforeseen challenges during the postoperative period.[13] Abdominal hernias are frequent in decompensated cirrhosis, and while elective repair is often deferred due

Risk factors influencing postoperative outcomes	
Surgical risk estimation in cirrhosis	Determined by liver disease severity, comorbidities, and surgery type
	Best assessed with cirrhosis-specific risk calculators plus clinical judgment
Key risk factors affecting surgical risk	Low MELD (6–9), low CTP (5–6), and no portal hypertension/ decompensation → minimal added risk
	Portal hypertension and decompensation (ascites, encephalopathy, varices) are major predictors of poor outcomes
	Standard labs (PT/INR, aPTT, PLT) do not reliably reflect bleeding/clotting risk in cirrhosis
	Very low PLT (<50–75k/μL) linked to bleeding and poor outcomes, but reflects severity of disease more than thrombocytopenia itself
	INR not independently predictive
	Nonhepatic comorbidities significantly affect outcomes
Preoperative evaluation	
Noninvasive fibrosis assessment	Use FIB-4/elastography in patients with unknown fibrosis stage. It might affect surgical planning
Prognostic risk models	VOCAL-Penn plus clinical judgment for preoperative risk is the preferred tool
Preoperative assessment for LT needs	For elective surgery, consider pre-op transplant evaluation if 90-day mortality risk > 15% (e.g., VOCAL-Penn)
Frailty	Assessing preoperative frailty helps refine risk prediction
Risk mitigation strategies and perioperative management	
Treatment of underlying liver disease	Manage reversible causes (HBV, HCV, autoimmune hepatitis) before elective surgery
Alcohol and tobacco cessation	Strict cessation lowers risk of liver events, infection, wound issues, and ICU need
Nutrition	Optimize with 30–35 kcal/kg/day and 1.25–1.5 g/kg/day protein ≥2 weeks pre-op; consider enteral feeding, or prehabilitation for frailty/sarcopenia if elective surgery
Peri-operative coagulopathy management	TEG is preferred over PT/INR to guide management
	Vitamin K/blood products have not been demonstrated to lower operative bleeding risk
Experienced centers	Refer to high-volume liver/transplant centers when possible
Surgery-specific considerations	
Abdominal hernia repair	Elective repair after ascites control reduces risk of emergent complications
Cholecystectomy	Laparoscopic favored in CTP A–B
	CTP C usually prohibitive. May benefit from supportive care and alternative drainage procedures
	VOCAL-Penn can guide decision-making in cases of uncertainty
Bariatric surgery	Safe in selected compensated cirrhosis; laparoscopic sleeve gastrectomy preferred
	In transplant candidates, may be done pre- or peri-transplant; limited data to support bariatric surgery post-transplant.

Table 1. Guideline recommendations and key concepts.

to bleeding risk, ascites, or poor nutrition, delaying repair increases the likelihood of emergent operations with markedly higher mortality.[14] For symptomatic cholelithiasis, laparoscopic cholecystectomy is favored in CTP A and B cirrhosis, but considered prohibitive in most CTP C cases.[15,16] In cardiac surgery, mortality ranges from 0%–11% in CTP A, and up to as high as 100% in CTP C.[17] Finally, bariatric surgery can be safe and effective in select compensated cirrhosis cases. In particular, sleeve gastrectomy is a safe procedure and can be considered prior to or after transplantation.[18]

COMMENTARY

Why Is This Important?

Patients with cirrhosis face some of the highest surgical risks, and until now, guidance towards the approach to perioperative management has been fragmented and inconsistent. This new ACG clinical guideline consolidates the evidence into a structured roadmap comparing risk calculators, CSPH evaluation, and procedure-specific considerations (see Figure 1) [1].

Key Study Findings

The guideline emphasizes that perioperative risk in cirrhosis depends on three domains: liver disease severity, comorbidities and surgery type. VOCAL-Penn is the preferred risk tool; MELD and CTP alone are insufficient.

CSPH is a strong predictor of adverse outcomes, even in compensated patients. Malnutrition, sarcopenia, and frailty are highly prevalent and strongly linked to postoperative mortality. Thus, nutritional optimization and prehabilitation are important risk mitigation strategies.

Elective hernia repair, laparoscopic cholecystectomy, and bariatric surgery can be safe in select patients with compensated cirrhosis, whereas cardiac surgeries require careful patient selection given the very high mortality associated with advanced liver disease. Regarding hemostatic derangements, the guideline suggests utilizing TEG to assess coagulopathy. The use of TPO agonists is reasonable in severe thrombocytopenic cases (<50K/mm3), but INR correction is not beneficial.

Finally, the guideline emphasizes the importance of multidisciplinary care and consideration of referrals to high-volume transplant-capable centers, while calling for more prospective data to refine perioperative risk prediction.

Caution

Most recommendations are based on low- to very-low-quality evidence, often from retrospective and single-center studies. VOCAL-Penn is validated only in patients who underwent surgery, which

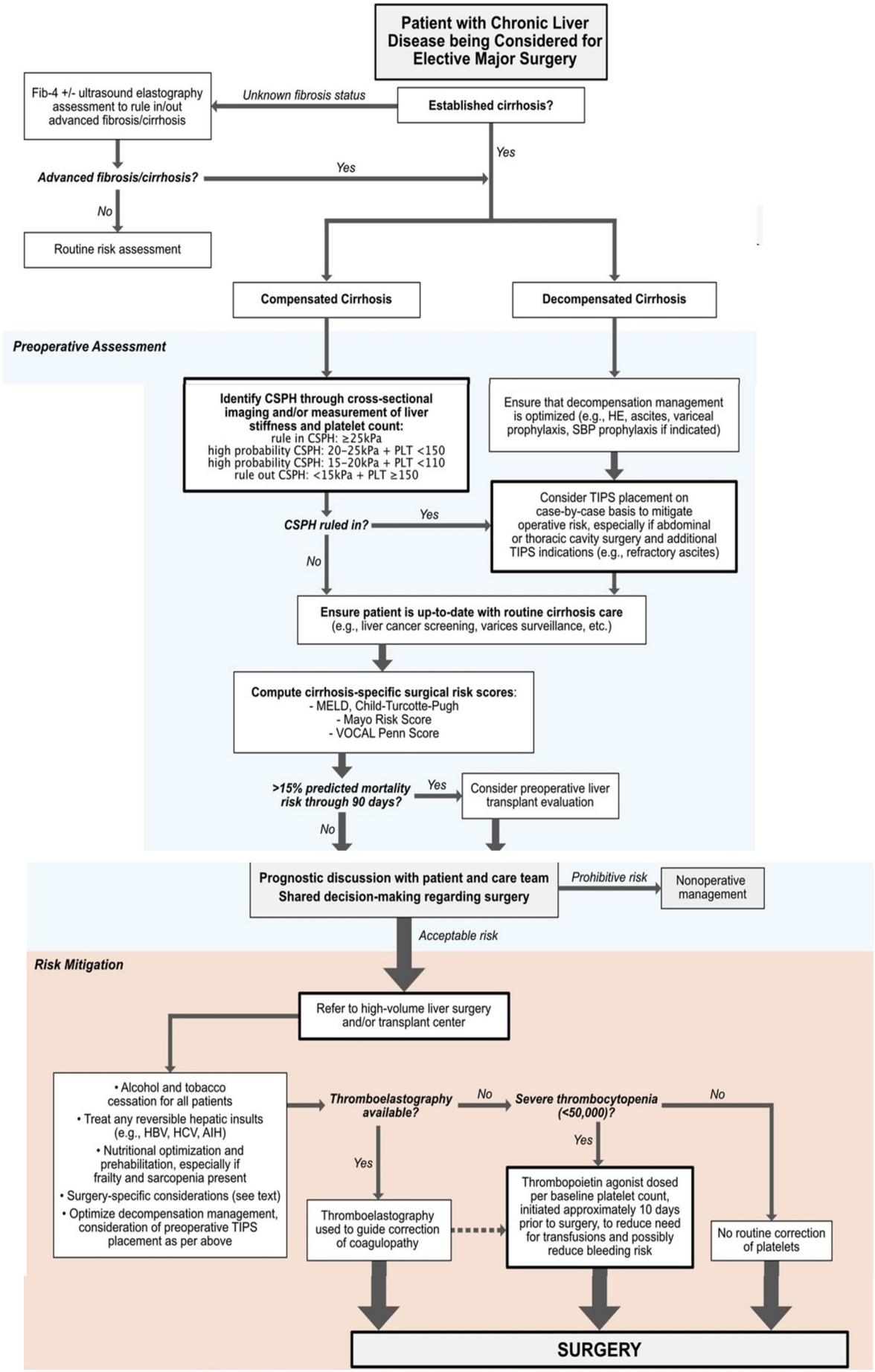

Figure 1. Proposed algorithm for cirrhosis surgical risk assessment and management.

may limit generalizability since it does not fully capture risk in those excluded from surgery. Ultimately, these scores cannot replace clinical judgment.

Lastly, procedure specific recommendations (e.g., hernia, cholecystectomy, cardiac, bariatric surgery) are often extrapolated from small or heterogeneous studies, so applicability may vary across different patient populations and practice settings.

My Practice

Depending on the type of procedure/surgery, I gauge the urgency of the pre-operative risk stratification. Though it may seem obvious, the first step is confirming that the patient truly has compensated advanced chronic liver disease, cACLD. If so, my next priority is determining whether CSPH is present. This is achieved through a comprehensive review of non-invasive liver disease assessments (NILDA), biochemical and radiographic parameters; occasionally, a biopsy is necessary, but I strive to avoid it if possible.

A few key questions I ask myself are: Is this surgery essential, and what is the surgeon's proposed timing? Is there flexibility here? Is the patient optimized as well as possible? Should we discuss this case with other consultants? Is a pre-operative TIPS or transplant evaluation needed in case they decompensate? What is the patient's functional status, and what is the status of their other chronic medical conditions? Is a pre-surgical debrief with all key providers involved needed? Do we need to clarify the utility of platelet, INR, and TEG assessment with the care team?

This last point is interesting as it is a very common question and often a point of contention. Although the decision is usually ultimately left to the person operating, I will show the team the data and describe the clear risk of increasing portal pressures without improving outcomes if unnecessary products are administered.

In my practice, I strive to approach these cases in a multidisciplinary manner, involving other specialists, including dietitians. If the patient is not ready for surgery and it is possible to delay, then this stance should be maintained when communicating with the primary surgical team.

Finally, I certainly use dot phrases in my practice when writing notes, but I think it's essential to review each part of these dot phrases with our patients (diet, exercise, medication, surveillance, lifestyle recommendations, etc.). Whether inpatient or outpatient, I believe it is essential to openly discuss the risks with the patient and empower them to be active in asking questions before deciding if and when to move forward with surgery.

For Future Research

The guideline highlights several areas where future research is urgently needed, including the development of prospective, multicenter studies to validate perioperative risk prediction models such as the VOCAL-Penn Score across diverse surgical settings, as well as studies clarifying the role of preoperative TIPS in reducing complications without worsening hepatic function.

There is also a need to determine the true impact of frailty and CSPH management on surgical risk. Although addressed in some studies, there remains a critical need to determine the impact of cirrhosis etiology on postoperative outcomes as well. These future directions will allow for a shift from expert consensus toward higher-quality, evidence-based recommendations that can guide surgical care in patients with cirrhosis.

Conflict of Interest

The authors do not have conflicts of interest to disclose.

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Updated 2025 ACG Clinical Guideline for the Management of Crohn's Disease

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IBD

This summary reviews Lichtenstein GR, Loftus EV Jr, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2025;120(6): 1225-1264.

Correspondence: Rahul S. Dalal, MD, MPH. Associate Editor. Email: EBGI@gi.org
Keywords: Crohn's disease; guideline; disease management

STRUCTURED ABSTRACT

Question: What are the major updates in the 2025 American College of Gastroenterology clinical guideline for the management of Crohn's disease (CD) compared with the 2018 guideline? How do these new guidelines incorporate recent therapeutic advances and evolving evidence into clinical practice?

Design: Evidence-based clinical practice guideline using the GRADE framework, incorporating systematic literature review and consensus expert opinion.

Setting: Multicenter, multidisciplinary guideline panel convened by the American College of Gastroenterology.

Patients: Adult patients with suspected, newly diagnosed, or established Crohn's disease, including luminal, fistulizing, and stricturing phenotypes.

Exposure or Interventions: Recommendations encompass diagnostic strategies, dietary and lifestyle interventions, corticosteroids, immunomodulators, biologics, and small molecule therapies, with special attention to new agents approved since the 2018 guidelines.

Outcomes: Induction and maintenance of clinical, endoscopic, and radiographic remission; prevention of complications; reduction in corticosteroid dependence; and patient-centered outcomes.

Data Analysis: Evidence was graded as high, moderate, low, or very low using the GRADE approach, with formulation of recommendations as strong or conditional.

Funding: American College of Gastroenterology.

Results: The 2025 updated guideline incorporates significant changes from 2018, reflecting both refinement in diagnostic approaches as well as therapeutic advances.

Diagnosis: The guidelines now provide a practical fecal calprotectin cut-off of >50-100 mg/g to distinguish inflammatory from non-inflammatory disease. It also formally endorses intestinal ultrasound (IUS) as a non-invasive, radiation-free adjunct for both diagnostic and monitoring, alongside other imaging techniques like CT or MR enterography.

Treatment. Most importantly, while mucosal healing on endoscopy remains the goal of therapy, the panel suggests against requiring patients to fail conventional therapies such as thiopurines or methotrexate before starting advanced therapies in moderate-to-severe CD, as new evidence emerged showing early intervention with advanced therapy is superior to accelerated step-up therapy.[1]

Mild-to-moderate CD. Mesalamine is now strongly discouraged for both induction and maintenance of luminal CD due to limited efficacy. Sulfasalazine should only be considered for patients with mild colonic CD. Budesonide at 9 mg daily remains recommended for induction in mild-to-moderate ileocecal CD but is recommended against for maintenance.

The role of dietary therapy is now recognized only in mild-to-moderate disease,

citing specific data from the DINE-CD trial, which supports Mediterranean or specific carbohydrate diets in select low-risk patients with mild disease, provided close monitoring is ensured.[2]

Moderate-to-severe CD. Systemic corticosteroids remain induction-only agents with a strong recommendation to limit use to fewer than 3 months, and to initiate a structured taper with rapid transition to steroid-sparing regimens.

Since 2018, the therapeutic landscape has expanded considerably, and the new guidelines incorporates new IL-23 inhibitors like risankizumab, guselkumab, and mirikuzumab, as well as JAK inhibitor upadacitinib alongside established agents such as anti-TNF therapies, vedolizumab, and ustekinumab for induction and maintenance. In particular, risankizumab is preferred over ustekinumab in patients previously exposed to anti-TNF agents. New subcutaneous infliximab and vedolizumab formulations are added as new maintenance options. No specific guidance for treatment selection is provided based on the location of the disease.

Fistulizing CD. Management of fistulizing disease has also broadened. Infliximab remains first-line therapy, but adalimumab, vedolizumab, ustekinumab, and upadacitinib are now considered reasonable options for induction.

Postoperative CD. Guidelines newly recommend endoscopic monitoring at 6-12 months after surgery. It continues to support continued observation in low-risk patients, but now adds vedolizumab, in addition to infliximab, to post-operative prevention regimens in high-risk patients.

COMMENTARY

Why Is This Important?

Since the 2018 guideline, multiple new biologic and small molecule agents have been approved for Crohn's disease, and data have emerged supporting earlier initiation of advanced therapies to improve long-term outcomes. The 2025 update reflects this shift toward early treat-to-target strategies, the de-implementation of ineffective agents, and individualized therapy selection based on disease phenotype, prior exposures, and patient preferences.

Key Study Findings

The update provides several practice-changing recommendations.

	Key Updates in 2025 Recommendations	What's New since 2018
Diagnostics	• Fecal calprotectin cut-off of 50–100 mg/g to differentiate inflammatory from noninflammatory colonic disease • Intestinal ultrasound offers a non-invasive, radiation free-method of assessing the bowel wall, mesentery, and adjacent structures and is an adjunct to the diagnosis and monitoring to therapy	• A fecal calprotectin threshold to differentiate noninflammatory disease. • IUS is formally endorsed to assess inflammation.
Mild-to-moderate CD	• Recommend against mesalamine for induction/maintenance • Recommend budesonide 9 mg daily for ileocecal induction but not for maintenance • For mild CD and low risk of progression, diet-based strategies along with careful monitoring for inadequate symptom relief, worsening inflammation, or disease progression may be considered	• A clear recommendation against the mesalamine for Crohn's disease • A clear recommendation against budesonide for maintenance • Recognition that diet-based strategies alone may be reasonable in select patients with mild disease and low risk of disease progression
Moderate-to-severe CD	• Suggest against requiring failure of conventional therapy before initiation of advanced therapy • Recommend oral corticosteroids for short-term induction of remission • Anti-TNFs remain foundational, but other recommended therapies include: Subcutaneous infliximab after IV induction; vedolizumab IV induction and SC for maintenance; ustekinumab for induction and maintenance; risankizumab; mirikizumab; guselkumab • Recommend the use of risankizumab over ustekinumab if there is prior exposure to anti-TNF therapy • Recommend upadacitinib use for induction and maintenance of remission for patients with moderate-to-severe CD who have prior exposure to anti-TNF	• A major shift away from step-up for moderate-severe Crohn's disease. • New suggestion of tapering rapidly to steroid-sparing agents and explicitly using a ≤3-month taper • Additional therapies are recognized including subcutaneous infliximab and vedolizumab for maintenance, and recognition of risankizumab, mirikizumab, and guselkumab as possible agents • New guidance on positioning risankizumab over ustekinumab in patients with prior anti-TNF exposure • Upadacitinib is also recommended for those with prior exposure to anti-TNF
Fistulizing CD	• Recommend infliximab use as induction therapy • Suggest the use of adalimumab, vedolizumab, ustekinumab, and upadacitinib for induction	• Expands prior recommendations with vedolizumab, ustekinumab, and upadacitinib as possible induction therapies

	Key Updates in 2025 Recommendations	What's New since 2018
Postoperative CD	• Recommend postoperative monitoring at 6–12 months over no monitoring • In patients with CD with low postoperative risk of recurrence, suggest continued observation as compared with immediate initiation of medical therapy for CD • In patients with high-risk CD, recommend anti-TNF therapy or vedolizumab to prevent postoperative endoscopic recurrence	• Formal recommendations on timing of post-operative monitoring • In addition to infliximab, vedolizumab is added as prophylaxis option in those with high risk of recurrence

Table 1. Key Updates in Recommendations.

First, it recommends against step-up approach, allowing clinicians to initiate advanced therapy for appropriate moderate-severe cases. Second, it strongly recommends against ineffective therapies like mesalamine, which remains common in community practice. Third, it strengths steroid stewardship by explicitly recommending less than 3 months of use. Fourth, it expands the treatment armamentarium including new IL-23 antagonists, JAK inhibitors, and subcutaneous formulations of infliximab and vedolizumab. Fifth, for perianal disease, the therapeutic options now extend beyond infliximab, as does for post-operative recurrence.

Caution

Despite these advances, many recommendations remain conditional and based on low-quality evidence, particularly concerning comparative positioning of agents and sequencing strategies after biologic failure. Evidence for dietary therapies also remain limited, and while they may benefit select motivated patients with low-risk disease, reliance on diet alone should not delay timely escalation in more severe phenotypes.

My Practice

In light of these updates, I will more readily consider initiating advanced therapies in treatment-naïve patients with moderate-to-severe CD, particularly those with high-risk features. Mesalamine will no longer be used in my practice for luminal disease. I will continue to be mindful of duration of corticosteroid use, and taper as soon as appropriate, with early transition to steroid-sparing maintenance therapies. With the expansion of IL-23 antagonists and upadacitinib as well as subcutaneous formulations of select advanced treatment, I will increasingly individualize treatment selection based on prior drug exposure, comorbidities, and patient preference for mode of administration.

For Future Research

Comparative effectiveness a nd head-to-head trials among newer biologics and small molecules are urgently needed, as are studies on sequencing strategies after treatment failure. Long-term safety data for JAK inhibitors in CD, and optimal dietary intervention protocols, are also priorities.

Conflict of Interest

None.

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Artificial Intelligence in Colonoscopy: Could It Be Making Us Worse?

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COLON

This summary reviews Budzyń K, Romańczyk M, Kitala D, et al. Endoscopist deskilling risk after exposure to artificial intelligence in colonoscopy: a multicentre, observational study. Lancet Gastroenterol Hepatol. 2025 Oct;10(10):896-903.

Correspondence: Margaret J. Zhou, MD. Associate Editor. Email: EBGI@gi.org
Keywords: Artificial intelligence; colonoscopy; observational study

STRUCTURED ABSTRACT

Question: Does exposure to artificial intelligence (AI) tools for colonoscopy impact non-AI assisted colonoscopy quality?

Design: Retrospective, observational study

Setting: Four endoscopy centers in Poland

Patients: This study included patients taking part in the ACCEPT (Artificial Intelligence in Colonoscopy for Cancer Prevention) trial. Patients were excluded if they had a contraindication to biopsy/polypectomy due to anticoagulant use or coagulation disorders, were pregnant, were referred for a known lesion, had a history of bowel resection or inflammatory bowel disease, or if the colonoscopy was not performed with a high-definition colonoscope.

Interventions: The 4 participating centers introduced AI computer-aided detection

(CADe) tools in late 2021, after which colonoscopies were randomly assigned to be conducted with or without AI assistance according to exam date. The AI system used was ENDO-AID CADe (OIP-1, Olympus Medical Systems, Tokyo). This study compared non-AI assisted colonoscopies performed 3 months before and 3 months after AI tools were implemented at these centers.

Outcomes: The primary outcome was the change in adenoma detection rate (ADR) of non-AI assisted colonoscopies before and after exposure to the AI tool. ADR included adenomas or cancers, but not sessile serrated lesions (SSLs). Secondarily, the authors measured the change in the mean number of adenomas per colonoscopy (APC) and the mean number of advanced APCs before and after AI exposure.

Data Analysis: ADR before and after AI exposure was compared using a χ^2 test. Mean number of APCs and advanced APCs before and after AI exposure was compared using a t-test. ADR was also compared by subgroups of center, physician specialty, and endoscopist sex.

Multivariable logistic regression was performed to identify variables affecting ADR with a random effect for endoscopist. Analyzed variables included patient age and sex, use of sedation, Boston Bowel Preparation Scale score, cecal intubation, endoscopist specialty (gastroenterologists vs surgeons), endoscopist's years after graduation from medical school, endoscopist sex, center, and AI implementation. Variables with a *P* value <0.05 in the univariable model were included in the adjusted multivariable model.

Funding: Authors of the study report financial support from the European Commission and the Japan Society for the Promotion of Science.

Results: Between September 2021-March 2022, 1,443 colonoscopies were performed without AI, of which 795 were performed before introduction of AI and 648 performed after. Colonoscopies were performed by 19 endoscopists (16 gastroenterologists and 3 general surgeons), who had performed >2,000 colonoscopies each with mean experience of 28 years (range 8–39).

Factors which had statistically significant differences between the patients in the before AI group vs those in the after AI group included higher proportion of female

patients (62% vs 55%, respectively; $P = 0.005$) and lower proportion of patients using sedation (77% vs 82%, respectively; $P = 0.02$) (**Table 1**).[1] Indications for colonoscopy were overall similar for alarm symptoms, surveillance, or positive fecal occult blood test.

ADR before vs after AI exposure decreased significantly from 28.4% to 22.4% (absolute difference -6.0% [95% CI -10.5 to -1.6%, $P = 0.009$]) (**Figure 1**). Mean APC before vs after AI exposure was not significantly different (0.54 vs 0.43; mean difference 0.11 [95% CI -0.01 to 0.24; $P = 0.071$]). Mean advanced APC was also similar (0.062 vs 0.063; mean difference -0.002, 95% CI -0.03 to 0.03; $P = 0.92$). Colorectal cancers were detected in 6 (0.8%) of colonoscopies before AI exposure vs 8 (1.2%) after AI exposure ($P = 0.35$).

Variables associated with a statistically significant change in ADR in multivariable logistic regression analysis included exposure to AI (adjusted odds ratio [aOR] 0.69; 95% CI 0.53-0.89; $P = 0.005$), male patient sex (aOR 1.78; 95% CI 1.38-2.30; $P < 0.0001$), and patient age ≥60 years (aOR 3.60; 95% CI 2.74-4.72; $P < 0.0001$).

COMMENTARY

Why Is This Important?

This is the first study to assess the impact of exposure to AI CADe on colonoscopy quality and physician performance in the absence of AI assistance. One of the posited risks of AI tools has been a decline in human-only colonoscopy quality, and this study provides important, novel observational data on how these AI tools may potentially negatively impact physician performance.

Prior evidence suggests that colonoscopy outcomes including ADR likely improve with CADe-assisted colonoscopy vs conventional colonoscopy. A recent systematic review/meta-analysis of 44 RCTs comparing CADe-assisted vs standard colonoscopy analyzing > 36,000 patients found higher ADR with CADe vs standard colonoscopy (44.7% vs 36.7%; rate ratio 1.21; 95% CI 1.15-1.28).[2] APC was also higher with CADe vs. standard colonoscopy (0.98 vs 0.78; incidence rate difference [IRD] 0.22; 95% CI 0.16-0.28). Examining 22 studies with > 19,000 patients, advanced colorectal neoplasia (ACN) detection rate was slightly higher with CADe (12.7% vs 11.5%; RR 1.16; 95% CI 1.02-1.32). This meta-analysis was used to inform the American Gastroenterological Association (AGA)'s

	Before AI introduction (n=795)	After AI introduction (n=648)	Total (n=1,443)	*P* value
Median age, years (IQR)	62 (46-70)	59 (44-70)	61 (45-70)	0.070
Sex				0.0046
Male	302 (38.0%)	294 (45.4%)	596 (41.3%)	—
Female	493 (62.0%)	354 (54.6%)	847 (5837%)	—
Sedation	613 (77.1%)	531 (81.9%)	1,144 (79.3%)	0.024
Adequate bowel preparation*	768 (96.6%)	627 (96.8%)	1,395 (96.7%)	0.87
Incomplete examination	4 (0.5%)	8 (1.2%)	12 (0.8%)	NA†
Indications				0.0090
Alarm symptoms‡	99 (12.5%)	78 (12.0%)	177 (12.3%)	—
Surveillance	119 (15.0%)	111 (17.1%)	230 (15.9%)	—
Positive faecal occult blood test	21 (2.6%)	11 (1.7%)	32 (2.2%)	—
Other §	277 (34.8%)	190 (29.3%)	467 (32.4%)	—
Unknown	279 (35.1%)	258 (39.8%)	537 (37.2%)	—

Table 1. Patient characteristics for those who had standard, non-AI assisted colonoscopies.
Data are n (%) unless other indicated.
*Defined by score of at least 6 on Boston Bowel Preparation Scale.
†Significant assessment was not done due to too few events.
‡Weight loss, anemia, GI bleeding signs, and tumor seen in CT scan.
§ Change in bowel habits or diarrhea.

living clinical practice guideline in 2025[3] which made no recommendation on the use of CADe-assisted colonoscopy, due to very low certainty of evidence on the impact of CADe-assisted colonoscopy on long-term outcomes such as colorectal cancer (CRC) incidence and mortality.

Interestingly, Budzyń et al pose the question of whether differences in ADR seen in prior studies of AI-assisted colonoscopy vs non-AI assisted colonoscopy as standard of care could in part be impacted by a possible reduction in ADR with unassisted colonoscopy seen after AI exposure. This hypothesis is difficult to support without delving more deeply into each study's design (including whether non-CADe colonoscopies were performed by endoscopists who had vs had not been exposed to AI tools). Nonetheless, the authors do cite an interesting study looking at the impact of a CADe system on visual gaze

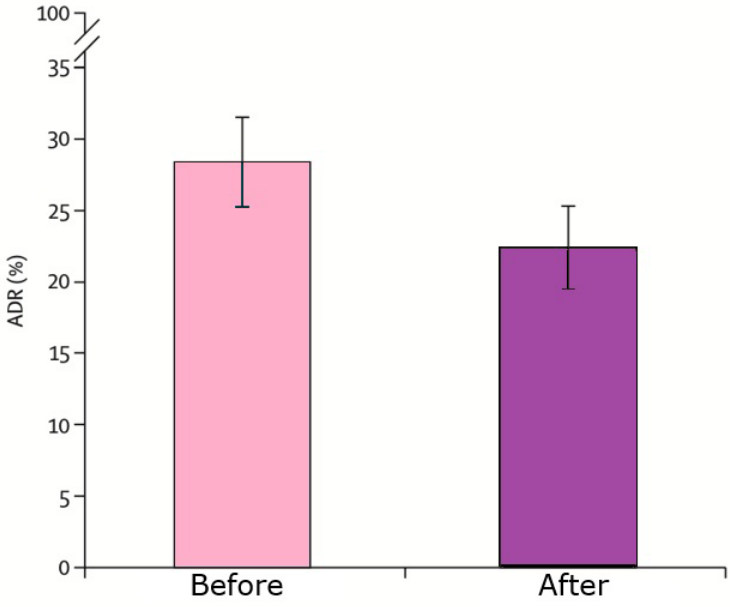

Figure 1. Change in ADR with standard, non-AI assisted colonoscopy before and after introduction of AI for polyp detection.

pattern assessed on colonoscopy video sequences, which found that use of CADe was associated with a significant reduction in eye travel distance compared to non-CADe exams.[4] While this study does not address the question of how any CADe exposure may impact endoscopist metrics, the potential impact on visual gaze could potentially be a mechanism by which prolonged CADe exposure could potentially impact performance over time. The trend towards potential decline in skills after AI exposure has been evaluated in other areas as well, including a recent study demonstrating that during the task of writing SAT essays, users of ChatGPT had the lowest neural engagement (assessed by electroencephalography) compared to those not using AI tools.[5] Further investigation into the impact of AI tools on human skills will continue to be important as AI is increasingly deployed in clinical practice.

Key Study Findings

Among 795 colonoscopies performed before and 648 performed after the introduction of AI, ADR before vs after AI exposure decreased significantly from 28.4% to 22.4% (absolute difference -6.0% [95% CI -10.5 to -1.6%, P = 0.009]).

Caution

The authors thoughtfully consider some limitations in this study, the most significant being that this was an observational study susceptible to confounding and selection bias. The study population was a nested cohort within a RCT, and the manuscript does not describe in detail the patient selection for those included in this study; specifically, it is not clear if all patients in the non-AI cohort after the introduction of the CADe tool were randomized into that group. A major concern for this study is potential differences in patient population between the groups before vs after AI introduction. Multiple variables demonstrated statistically significant differences between the two groups, which the authors adjusted for in their analysis; however there is likely still residual confounding. Furthermore, results were obtained from only 19 endoscopists of at least moderate experience level which

may limit generalizability, and there were insufficient colonoscopies to allow per-endoscopist analyses. Importantly, withdrawal time was not reported in this study, which could potentially significantly impact ADR. ADR for this cohort was also quite low (overall ADR among the 1,443 colonoscopies performed without AI was 25.7%). While Poland does not have set ADR targets as is seen in the U.S., generalizability of these study results to endoscopists in the U.S. who now have an ADR target of 35% may be limited.

My Practice

My institution currently does not use any CADe system for colonoscopy. A 3-month trial of a CADe device (GI Genius; Medtronic, Minneapolis, MN) at my institution was previously described,[6] where a retrospective pragmatic trial was conducted at our outpatient endoscopy unit. In contrast to many prior studies, we saw no statistically significant difference in ADR with vs without CADe (40.1% vs. 41.8%; OR 1.14; 95% CI 0.83-1.56; $P = 0.41$) or in mean APC (0.78 vs 0.89; OR 1.08; 95% CI 0.80-1.45; $P = 0.63$). Based on these findings, our endoscopy unit did not continue with the CADe system, although this remains under active discussion.

With or without the CADe system, I prioritize using best practices for a high-quality colonoscopy.[7] First, our unit uses split prep for all patients. During the procedure, I take care to maximize mucosal exposure by irrigating and using an Endocuff, and either perform a second look or retroflex in the right colon. Our endoscopy unit has a robust Colonoscopy Quality Assurance Program[8] which monitors and reports endoscopist ADR, SSL-DR, and withdrawal times with steps to improve performance among endoscopists with lower detection rates.

For Future Research

Prospective trials comparing colonoscopy quality before vs after AI exposure are needed to validate these findings. These studies should evaluate outcomes including ADR and APC as well as other patient-important outcomes such as sessile serrated lesion (SSL) detection rate and CRC incidence.

Conflicts of Interest

Dr. Zhou reports no conflicts of interest related to this study.

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EVIDENCE-BASED GI
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Semaglutide for the Treatment of Metabolic Dysfunction-Associated Steatohepatitis

HEPATOLOGY

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This summary reviews Sanyal AJ, Newsome PN, Kliers I, Østergaard LH, Long MT, Kjær MS, Cali AMG, Bugianesi E, Rinella ME, Roden M, Ratziu V; ESSENCE Study Group. Phase 3 Trial of Semaglutide in Metabolic Dysfunction-Associated Steatohepatitis. N Engl J Med. 2025 Jun 5;392(21):2089-2099.

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Keywords: obeticholic RCT, semaglutide, MASH, GLP-1

STRUCTURED ABSTRACT

Question: The goal of this phase 3 trial was to evaluate the efficacy and safety of once-weekly subcutaneous semaglutide for the treatment of metabolic dysfunction–associated steatohepatitis (MASH).

Design: This was an ongoing phase 3, multicenter, randomized, double-blind, placebo-controlled trial. The reported results are from a planned interim analysis (Part 1) conducted at week 72.

Setting: The trial was conducted at 253 clinical sites across 37 countries.

Patients: The interim analysis included 800 patients with biopsy-defined MASH and liver fibrosis stage 2 or 3. Patients were aged ≥ 18 years.

Exposure: Patients were assigned in a 2:1 ratio to receive once-weekly subcutaneous semaglutide at a dose of 2.4 mg or a placebo for 240 weeks.

Outcomes: The primary endpoints for Part 1 of the trial were: 1) resolution of steatohepatitis without worsening of liver fibrosis defined as an NAS of 0 for ballooning and 0 to 1 for inflammation, and 2) reduction in liver fibrosis without worsening of steatohepatitis defined as at least a 1-stage reduction on the NASH CRN fibrosis scale.

Data Analysis: Efficacy analyses were based on the intention-to-treat principle. Statistical significance was determined using a graphical testing strategy with a two-sided level of $P < 0.0045$. Missing data were handled using reference-based multiple imputation.

Funding: The study was funded by Novo Nordisk.

Results: The first primary endpoint (resolution of steatohepatitis without worsening of fibrosis) was met, occurring in 62.9% of the semaglutide group vs 34.3% of the placebo group ($P < 0.001$). The second primary endpoint (reduction in liver fibrosis without worsening of steatohepatitis) was also met, occurring in 36.8% of the semaglutide group versus 22.4% of the placebo group ($P < 0.001$). Additionally, patients in the semaglutide group showed significant weight loss (mean change of -10.5%) compared to the placebo group (mean change of -2.0%). Gastrointestinal adverse events (e.g., nausea, diarrhea) were more common in the semaglutide group, but no new safety signals were identified.

COMMENTARY

Why Is This Important?

The glucagon-like peptide-1 receptor agonist (GLP-1 RA) semaglutide is a known treatment for type 2 diabetes and obesity. Multiple studies have also demonstrated the benefit of semaglutide in reducing the risk of major adverse cardiovascular events (MACE), a composite outcome that includes cardiovascular death, nonfatal myocardial infarction, and stroke, and these benefits have been demonstrated regardless of diabetes.[1,2] In addition, improved heart failure outcomes and reduction of major renal outcomes have also been demonstrated.[3,4] The Essence trial provides strong evidence that semaglutide can also effectively treat MASH with fibrosis, a severe form of liver disease that is closely linked to metabolic dysfunction.[5] The findings are significant because they demonstrate both histologic improvements in the liver (resolution of steatohepatitis and a reduction in fibrosis) and broader cardiometabolic benefits like weight loss and improved glycemic control. This dual action addresses a major unmet need for a treatment that can target both the liver disease and its underlying causes.

Compared to placebo, semaglutide significantly improved liver histologic results with resolution of steatohepatitis without worsening of liver fibrosis occurring in 62.9% of the semaglutide group, compared to 34.3% in the placebo group.

Key Study Findings

In addition, a reduction in liver fibrosis without worsening of steatohepatitis was seen in 36.8% of the semaglutide group versus 22.4% in the placebo group, and a combined resolution of steatohepatitis and a reduction in liver fibrosis was reported in 32.7% of patients in the semaglutide group, compared to 16.1% in the placebo group.

Other beneficial effects included a mean change in body weight of -10.5% for the semaglutide group versus -2.0% for the placebo group and semaglutide also appeared to be associated with improvements in glucometabolic factors and noninvasive markers of liver health. The percentage of patients who had an adverse event was 86.3% in the semaglutide group and 79.7% in the placebo group. Adverse events leading to discontinuation were 2.6% for semaglutide and 3.3% for placebo.

Caution

While the results are promising, the study is ongoing. The full long-term clinical outcomes are not yet available. A small number of patients dropped out, which could impact the final analysis. The trial had a small representation of Black patients and a small number of lean patients, so the findings may not be generalizable to these populations.

My Practice

The findings of this trial suggest that semaglutide could become a key therapeutic option for patients with MASH, particularly those with stage 2 or 3 fibrosis. Indeed, many patients with MASH and MASLD are already taking semaglutide or other GLP-1 RAs given the high prevalence of MASLD and MASH in those with type 2 diabetes. On August 15, 2025, the FDA granted approval for semaglutide as a treatment for adults with moderate to advanced fibrosis. Unlike the Phase 2 trial with semaglutide, in this study, semaglutide demonstrated significant improvements in both MASH activity and fibrosis, rather than MASH resolution alone.[6] This is the second approved therapy after resmetirom, a beta thyroid hormone agonist, which was approved in March 2024 for the same population of MASH patients. In my practice, the vast majority of my patients with MASH have features of metabolic syndrome, including type 2 diabetes, and I routinely work with referring physicians to incorporate GLP-1 RA therapies for diabetes and obesity, given previous findings demonstrating improvement in MASH activity as well as the other metabolic benefits and weight loss. The Essence Trial demonstrated, for the first time, improvement in fibrosis with semaglutide, a key endpoint in the treatment of individuals with MASH and moderate to severe

fibrosis. Practicing gastroenterologists now have 2 approved options for pharmacological treatment of MASH in addition to lifestyle interventions.

For Future Research

Future research should focus on the long-term clinical outcomes of semaglutide treatment, including its effects on cirrhosis-free survival, which will be reported in part 2 of this trial. Longer-term prospective studies are also required to explore the role of semaglutide and other GLP-1 RAs in the treatment of those with cirrhosis, which will be important given retrospective administrative database studies suggesting GLP-1 RAs can reduce rates of hepatic decompensation.[7]

Combination therapies with GLP-1 RAs and other MASH therapies and other mechanisms of action, including beta thyroid agonists such as remetirom, will also be important given the pleiotropic mechanisms involved in the pathogenesis of MASH.[8]

Disclosures

Dr Kwo reports the following: Consultant for AbbVie, Durect, Genentech, HepQuant, Inventiva, Mirum, PB Gene, Tune Therapeutics; Advisory Board: Aligos, Amgen, Arbutus, Ausper Bio, Galapagos, Gilead, Novo Nordisk, Ocelot, Salix, Surrozen; Research Grant: Altimmune, Gilead, Inventiva, Novo Nordisk; Target Registries, Ultragenyx, Akero, 89Bio Vir Bio; Grant Support: Ausper Bio, Madrigal, Salix, Takeda; Stockholder: Durect.

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